## **Abstract**

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Methods and compositions are provided for the identification of expression signatures in ER+ breast cancer cases, where the signatures correlate with responsiveness, or lack thereof, to treatment with tamoxifen or another antiestrogen agent against breast cancer. The signature profiles are identified based upon sampling of reference breast tissue samples from independent cases of breast cancer and provide a reliable set of molecular criteria for predicting the efficacy of treating a subject with breast cancer with tamoxifen or another antiestrogen agent against breast cancer. Additional methods and compositions are provided for predicting responsiveness to tamoxifen or another antiestrogen agent against breast cancer in cases of breast cancer by use of three biomarkers. Two biomarkers display increased expression correlated with tamoxifen response while the third biomarker displays decreased expression correlated with tamoxifen response.